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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Paper No. 22

Application Number: 08/757904

Filing Date: November 27, 1996

Appellant(s): Edwin Wegman et al.

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Roland Plottel  
For Appellant

**EXAMINER'S ANSWER**

This is in response to appellant's brief on appeal filed June 4, 1998.

**(1) Real Party in Interest**

A statement identifying the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

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**(3)     *Status of Claims***

The statement of the status of the claims contained in the brief is correct.

**(4)     *Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5)     *Summary of Invention***

The summary of invention contained in the brief is correct.

**(6)     *Issues***

The appellant's statement of the issues in the brief is correct.  
Appellant's brief includes a statement that claims do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

**(7)     *Grouping of Claims***

**(8)     *ClaimsAppealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(9)     *Prior Art of Record***

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5424208

Lee et al.

6-1995

Guidicelli, Y. et al. "Influence of Trypsin on Lipolysis in Human Fat Cells Comparison with Rat Adipocytes." Biochimica et Biophysica Acta, vol. 450 (1976), pp. 358-366.

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**(10)    *Grounds of Rejection***

The following ground(s) of rejection are applicable to the appealed claims:

1.      Claims 1-20 are rejected under 35 U.S.C. § 103 as being unpatentable over Lee et al. combined with Guidicelli et al.

Claims 1-19 are drawn to the reduction of adipose tissue at selected sites in the body comprising the introduction of collagenase and another proteinase into said tissue. Claim 20 is drawn to a method of reducing adipose tissue for cosmetic purposes.

Lee et al. teaches that collagenase plus chymopapain digests connective tissue. Adipose tissue is particularly disclosed as being effectively digested so as to obtain endothelial cells present therein. Guidicelli et al. discloses that it is conventional to use collagenase and trypsin for the purpose of digesting and isolating adipocytes.

The disclosure of the Lee et al. patent is drawn to proteolytic enzyme composition containing collagenase "useful for hydrolyzing connective tissue in biological systems." See col. 3, lines 60-65. Further, at col. 5, lines 20-33, the patent states that "the teachings of the present invention [are] widely applicable in a number of tissue digestion procedures including those which involve in vivo digestion . . ." While it is clear that the in vivo digestion of adipose tissue was not expressly disclosed, the teaching of a U.S. patent is not limited to its preferred embodiments. The prior art shows that connective tissue, including adipose tissue, may be digested by use of a collagenase-containing proteolytic composition and that such composition is conventionally administered in vivo for the exact purpose of dissolving a broad range of different types of

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connective tissue. It is noted that the Lee et al. reference discloses the effects of the claimed composition both in vitro and for in vivo application for the digestion of connective tissue wherever desired and as the claims call only for the reduction of adipose tissue, it would have been obvious and predictable to one of ordinary skill in the art to use conventional enzymes known to digest said tissue, regardless of its site the expected digestion, i.e. dissociating the cells of the tissue. The term "tissue" is defined as "an aggregation of morphologically and functionally similar cells" and "cellular matter regarded as a collective entity." As a result of disaggregation of these cells by dissolution of the connective tissue matrix, the tissue has been digested and therefore its amount has been reduced. Such is clearly taught as predictable from the teaching of Lee et al. such that one of ordinary skill in the art would expect that, should he/she wish to reduce the amount of any connective tissue, including adipose tissue, at a site in the body, one would be motivated to use a composition well known to digest said tissue with a reasonable expectation of success. It is noted that absolute predictability is not required under the standard of obviousness of 35 USC 103; all that is required is a reasonable expectation of success. In re Long, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Finally, with regard to claim language drawn to "for cosmetic purposes", such language fails to patentably distinguish the claims over the disclosure of Lee et al. The term "cosmetic purposes" may be defined to be so broad as to include such a wide range of applications such as treatment of fatty cysts such that one of ordinary skill in the art would be motivated as disclosed and taught in the patent to digest the connective tissue, i.e. adipose tissue, contained therein with a reasonable expectation of success of said digestion,

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thereby reducing the adipose tissue at said site. Optimization of dose is deemed well within the skill of the practitioner as the enzyme kinetics of collagenase and other enzymes are well known and dose may be extrapolated based upon amount of substrate desired to be digested.

**(11) Response to Argument**

It appears that the difference between Appellants' position in this dispute and the Examiner's position is one of claim interpretation. Appellants have continually asserted throughout the prosecution history of this application that Appellants' invention is "an alternative to surgical liposuction" (see the specification, page 2, lines 10-13); however, as stated previously by the Examiner, the claim language is not so limiting and further, such has not been shown.

Appellants admit at page 4 of the Appeal Brief that "Lee et al. use collagenase and chymopapain to digest connective tissue." There is no dispute that Lee teaches that 1) adipose tissue is classified as a connective tissue, 2) collagenase can digest adipose tissue and 3) collagenase has been used *in vivo* for the purpose of digesting various different connective tissues (see Lee et al., col. 5, lines 22-33).

Once again, Appellants assert that because Lee et al. does not explicitly disclose the *in vivo* use of collagenase with adipose tissue, "the present invention cannot be derived from Lee et al." and that "Lee et al. do not suggest to use their mixture in vivo as an alternative to liposuction."

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As stated in previous office actions, Appellants' characterization of both the claim language and the Lee et al. reference is much too narrow. The claim language recites that to reduce adipose tissue at a selected site in the body one administers to that adipose tissue collagenase or collagenase in conjunction with other proteinases so that the adipose tissue at the site is reduced. This method may be practiced for cosmetic purposes. This is all that is required of the claimed method.

In the analysis of the claim language, it is noted that Applicants claim the administration of collagenase to adipose tissue, which is defined as a type of connective tissue which is areolar connective tissue in which the nutrient-storing function is greatly increased. The storage cells are called adipocytes and are the main component of the tissue mass. The adipocytes contain pure neutral fat in the form of oil which occupies most of the cell's volume. Very little matrix is present in adipose tissue and the tissue is richly vascularized due to the need to deliver fat to and from the storage tissue.

Lee et al. teaches that collagenase plus chymopapain digests connective tissue. Adipose tissue is particularly disclosed as being effectively digested so as to obtain endothelial cells present therein. Guidicelli et al. discloses that it is conventional to use collagenase and trypsin for the purpose of digesting and isolating adipocytes. This teaching indicates that the collagenase is effective in hydrolyzing the matrix which holds the cells together.

Appellants' address the disposition of the fat in the body, comparing what is asserted to take place in vivo versus what happens in vitro. They suggest that col. 8, lines 45-51 provides

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evidence that all the adipocytes survive intact. However, it is noted that a supernatant is present which is also pipetted away and no evaluation of this supernatant is disclosed. As both Appellants and Lee et al. are treating the same type of tissue with the same composition, it is expected that in both cases the resulting hydrolysis of the matrix that at least some of the fat cells will be damaged and disrupted, thereby releasing the oil within.

Appellants argue that "there is nothing in Lee et al. to suggest that their enzymes be used to digest the connective tissue of adipose tissue in vivo, or if that were done, that a substantial amount of adipose tissue would disappear from the site." Once again, the analysis of the claim language is too narrow and, if the latter part of the statement is to be interpreted as an argument for unexpected result, such has not been shown. Appellants' use of the phrase "the connective tissue of adipose tissue" is not clear. As stated previously, adipose tissue is a connective tissue itself. In further analysis of the claim language, it is noted that the claims only require that the amount of adipose tissue at a selected site be reduced. The term "tissue" is conventionally defined as "an aggregation of morphologically and functionally similar cells" and "cellular matter regarded as a collective entity." As a result of disaggregation of these cells by dissolution of the connective tissue matrix, the tissue has been digested and therefore its amount has been reduced. If the adipocytes are in the least not in the form and function of a tissue, i.e. a group of cells that are similar in structure and perform a common function held together by a matrix, no adipose tissue exists. As stated above, it is clear from the disclosure of Lee and Guidicelli that the effects of collagenase on adipose tissue result in the disruption of the tissue into cells and cell debris and

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therefore, whether in vitro or in vivo, collagenase reduces the amount of adipose tissue to which it has been applied.

Appellants' assert at page 6 of the Appeal Brief that "in applicants' invention, the body itself removes the released fat from the selected location of treatment, resulting in less fatty material there. This disappearance of fat from the selected locations provides the desired cosmetic result. It could not be predicted from Lee et al." However, once again the claims are not so limiting. First, there is no limitation as to the "disappearance of fat from the selected locations". All that is claimed is that the amount of adipose tissue be reduced. Once the adipocytes are disaggregated and no longer in the form of a tissue, this limitation is met. Such a result is clearly suggested as predictable by the disclosure of Lee et al. Second, there is no limit on the amount or volume of adipose tissue to be treated. Therefore, claims to the percentage of the adipose tissue reduced as a result of the treatment are dependent upon the amount of tissue treated in the first place. Finally, the term "for cosmetic purposes" fails to define the claims over the prior art. These cosmetic purposes include such a wide range of applications such as treatment of small fatty cysts such that one of ordinary skill in the art would be motivated as disclosed and taught in the patent to digest the connective tissue, i.e. adipose tissue, contained therein with a reasonable expectation of success of said digestion, thereby reducing the adipose tissue at said site.

Appellants argue that the phrase "the body metabolizing fat released from said adipose tissue" creates another limitation which is not suggested by Lee et al. and that the Examiner has

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ignored the experimental data. First, it is never been shown in the experimental data as to how much fat (not tissue) is released as a result of the claimed method or that the bodies of the rats treated with the collagenase metabolized any of fat released. Any practitioner in the art would be aware that in the disruption of any tissue, either enzymatically or physically, some of the cells located therein will be damaged and/or destroyed. This would have been particularly expected with adipose tissue because, as state above, the adipocytes are actually nothing more than cellular storage bags of oil. Further, any practitioner in the art is aware of the basic facts regarding the body's metabolism. Dependent upon the basal metabolic rate and the caloric intake of the animal, ingested food is used either immediately for energy or stored as fat. It is only during a reduced caloric intake which will not meet the metabolic needs of the individual that fat is released from adipose tissue and metabolized for energy. It is noted that during all phases of the experiments performed by Appellants that the rats were fed ad libitum. Further, all rats were necropsied on days 2-4 after injection and per Table 1, page 22, of the specification, there was no change in the weights of the rats from pre-injection to pre-sacrifice. Finally, evaluations of the fat pads were done by either visible inspection for degree of tissue disruption and/or weight of the pads of adipose tissue. It is well accepted by any practitioner, and in fact by anyone who has ever engaged in a weight-reducing diet, that the metabolism of fat, even in the face of starvation, takes place over a period of weeks and certainly not in two to four days. As fat has mass and therefore weight, and as the weight of the rats never changed, Appellants' assertions that the fat has been metabolized is simply not supported by any evidence of record. Further, there is no limitation as

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to the amount of fat which must be metabolized as a result of the claimed invention, and therefore, if even a small amount of that released from the adipose tissue is metabolized, such has met the claim limitations.

Appellants argue that the disposition of the intact and ruptured adipocytes is “a vital part” of the claimed invention and that “reducing the amount of adipose tissue at the selected locations includes its disposal.” Appellants accuse the Examiner of not reading the claims in their entirety and not giving the words their plain meaning. Such is not well taken. All of the definitions cited above and in previous office actions have been taken word for word from conventional physiology textbooks; therefore, the Examiner has been giving the words their plain meaning in the art. It appears that Appellants are reading limitations into the claims that are not in fact present.

Once again Appellants represent their invention as an alternative to liposuction and compare it in terms of safety. However, such has never been claimed. Liposuction is an art-recognized procedure for removal of excessively enlarged fat deposits. A conventional liposuction procedure removes about anywhere from 1 to 2.5 liters of fat from a patient and in some large volume liposuctions, upwards of 5 liters of fat. While it is the position of the Examiner that there is no limit upon the volume of adipose tissue to be treated, the Examiner has based the motivation and predictability of the efficacy of the claimed invention from the Lee reference on small amounts of adipose tissue such as found in fatty cysts. If Appellants’ arguments regarding the comparison to liposuction be intended and taken for evidence of unexpected result, it is also the position of the Examiner that such has not been shown. There is

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absolutely no support in the evidence of record that the treated fat pads represent the volume of adipose tissue conventionally removed by liposuction and further, there is absolutely no evidence that the body would or even could metabolize 2.5 liters of fat released as a result of the collagenase treatment.

Finally, Appellants' characterization of claims 19 and 21 as separately patentable because they "recite numerical limits on the amount of reduction of adipose tissue at the selected locations" are not found to be persuasive as the percentage of the adipose tissue reduced as a result of the treatment are dependent upon the amount of tissue treated in the first place.

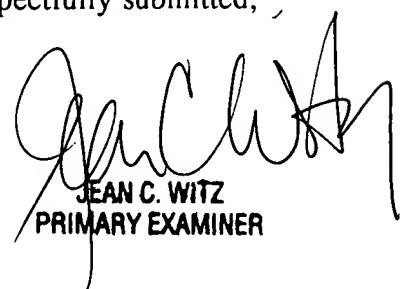
In view of the prior art, one of ordinary skill in the art would expect that, should he/she wish to reduce the amount of any connective tissue, including adipose tissue, at a site in the body, one would be motivated to use a composition well known to digest said tissue with a reasonable expectation of success. It is noted that absolute predictability is not required under the standard of obviousness of 35 USC 103; all that is required is a reasonable expectation of success. In re Long, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Optimization of dose is well within the skill of the practitioner as the enzyme kinetics of collagenase and other enzymes based upon amount of substrate are well known.

For the above reasons, it is believed that the rejections should be sustained.

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Michael G. Wityshyn  
Supervisory Patent Examiner  
Technology Center 1600

Respectfully submitted,

  
Jean C. Witz  
PRIMARY EXAMINER